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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,501	OGATA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *12-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/31/01; 4/2/02;*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-22 are pending.

2. Applicant's election with traverse of Group I, Claims 1-11 drawn to a method of maintaining or increasing low vasopressin level comprising administering to a patient at least one substance that inhibits the binding between PTHrP and a receptor thereof, filed 2/3/04, is acknowledged. The traversal is on the grounds that (1) the claims cover methods of maintaining or increasing low vasopressin level via inhibition of binding between PTHrP and a receptor thereof. Yamamoto et al use an in vitro system to characterize the effects of fragments of PTHrP on the rat suproptic nucleus (SON). The coronal hypothalamic slices containing the SON are artificially perfused with the PTHrP fragment. Further, the receptor for PTHrP that mediates this effect, which the authors allege is "distinct" from already identified PTHrP receptors, has not been identified. Applicants have demonstrated that levels of vasopressin, which are below normal in a hypercalcemia model, can be increased using antibodies against PTHrP. Applicants submit that the claims share the same special technical feature and request that the restriction requirement be withdrawn. This is not found persuasive because of the reasons set forth in the restriction mailed 12/3/03. Yamamoto *et al* (Endocrinology 138(1): 383-388; PTO 892) teach a method of increasing low vasopressin level in a patient such as rat by administering to said patient at least one substance such as PTHrP (1-34) (See Fig 1, in particular). The reference method inherently inhibits the binding of PTHrP to a receptor and thereby increasing the vasopressin level. The reference further teaches a method of maintaining vasopressin level by administering to said patient a substance such as an antagonist to PTHrP such as PTHrP (7-34) or PTH (1-34) (See Fig 2, page 387in particular). Further, a prior art search also requires a literature search. It is a burden to search more than one invention. Therefore, the requirement of Group I and Groups II-IV is still deemed proper and is therefore made FINAL.

3. Claims 12-22 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-11 are being acted upon in this Office Action.

5. The reference 09/269,332 cited on PTO 1449 filed 3/28/02, and references 09/423,800 and 09/720,326 cited on PTO filed 3/18/03 have been considered but crossed out because they are not appropriate for printing on issue patent.

6. The STIC system branch has deleted the non ASCII characters of sequence 12-14 in CFR filed 12/31/01.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the monoclonal antibodies produced by hybridomas #23-57-137-1 (claim 6) is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification.

If it is not so obtainable or available, a deposit of hybridomas secreting said monoclonal antibodies may satisfy the enablement requirements of 35 U.S.C. 112, first paragraph. See 37 CFR 1.801-1.809.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridomas secreting said antibodies have been deposited under the Budapest Treaty and that the hybridomas will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or **for the enforceable life of the patent whichever is longer**. See 37 CFR 1.806.

If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be

made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

If the deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which case the statement need not be verified. See MPEP 1.804 (b).

Further, the specification does not provide sufficient guidance for a method of making and using *any* "substance that inhibits the binding of PTHrP and its receptor" (claims 1 and 9), *any* "PTHrP receptor antagonist" (claim 2), any anti-PTHrP antibody (claim 3), *any* fragment of any anti-PTHrP antibody (claim 4), *any* modified form of *any* fragment of anti-PTHrP antibody" (claim 4), any humanized or chimeric PTHrP antibody (claim 5) for the claimed methods of maintaining or increasing low vasopressin level or treating at least one symptom such as polyuria, dehydration, mouth dryness and hyperosmolarity caused by a decrease in vasopressin level.

The specification discloses only a method of maintaining or increasing low vasopressin level comprising administering to a patient only monoclonal antibody against human PTHrP selected from the group consisting of anti-PTHrP (1-34), monoclonal antibody produced by hybridomas #23-57-154, #23-57-137-1, humanized or chimeric antibody against human PTHrP.

The specification does not teach how to make, much less how to use any "substance" and "PTHrP antagonist" that inhibit the binding between PTHrP and any receptor thereof because the terms "substance" and "antagonist" without the amino acid sequence has no structure, much less function. Further, there is insufficient in vivo working example demonstrating all undisclosed substance and antagonist would inhibiting the binding of PTHrP to its receptor, let alone increasing low vasopressin level.

Stryer *et al* teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions could result in substantially different pharmacological activities. Given the indefinite number of undisclosed "substance", "antagonist", it is unpredictable which undisclosed substance or antagonist would bind to PTHrP or which PTHrP receptor, in turn, would be useful for maintaining or increasing low vasopressin level when administered to a patient.

Even if the claimed method is limited to antibody, Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. In addition to the lack of guidance as to which fragment of which PTHrP antibody is effective for the claimed method, there is insufficient guidance about how to modify which "fragment" in the undisclosed substance or antibody fragment, such as which amino acid within the binding region of the antibody or the substance to be substituted, deleted or added and whether the resulting modified fragment, or substance would still binds to PTHrP receptor, in turn, is effective for a method of maintaining or increasing low vasopressin level.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Further, the specification discloses only monoclonal antibody that binds to human PTHrP (1-34) consisting of SEQ ID NO: 75, the binding specificity of other monoclonal antibody, fragment thereof, chimeric and humanized antibody are not enabled.

Since the binding specificity of the antibody in the claimed methods is not enabled, it follows that any monoclonal antibody, any antibody fragment instead of the binding fragment, chimeric antibody, and humanized antibody for the claimed methods are not enabled.

9. Claims 1-5 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** for a method of making and using *any* "substance that inhibits the binding of PTHrP and its receptor" (claims 1 and 9), *any* "PTHrP receptor antagonist" (claim 2), any anti-PTHrP antibody (claim 3), *any* fragment of any anti-PTHrP antibody (claim 4), *any* modified form of *any* fragment of anti-PTHrP antibody" (claim 4), any humanized or chimeric PTHrP antibody (claim 5) for the claimed methods of maintaining or increasing low vasopressin level or treating at least one symptom such as polyuria, dehydration, mouth dryness and hyperosmolarity caused by a decrease in vasopressin level.

The specification discloses only a method of maintaining or increasing low vasopressin level comprising administering to a patient only monoclonal antibody against human PTHrP selected from the group consisting of anti-PTHrP (1-34), monoclonal antibody produced by hybridoma #23-57-154, #23-57-137-1, humanized or chimeric antibody against human PTHrP.

With the exception of the specific monoclonal antibodies that binds to human PTHrP1-3 of SEQ ID NO: 75, there is insufficient written description about the structure associated with function without the amino acid sequence of *any* "substance capable of inhibiting the binding between PTHrP and any receptor", and *any* "PTHrP antagonist". Even if the claimed method is limited to antibody that binds to human PTHrP (1-34) of SEQ ID NO: 75, the binding specificity of the other antibody such as anti-PTHrP antibody, monoclonal antibody, humanized antibody, chimeric antibody, any fragment of any anti-PTHrP antibody, and "modified form of any fragment" are not adequately described.

Further, the specification discloses only antibody that binds to only human PTHrP (1-34) of SEQ ID NO: 75. Given the lack of any additional parathyroid hormone related peptide (PTHrP) to which the antibody binds in the claimed method, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "a receptor thereof " in claims 1 and 9 is indefinite and ambiguous because it is not clear which receptor that can bind to PTHrP that the substance inhibit in the claimed method since there is more than one receptors to which the PTHrP binds.

The "fragment of anti-PTHrP antibody" in claim 4 is ambiguous and indefinite because antibody has the binding fragment and the Fc fragment and it is not clear which fragment of the antibody applicant intends to claim. In addition to the problem with the fragment, it is not clear which "modified form of the fragment" that is part of the claimed invention. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "#23-57-137-1 antibody" in claim 6 is merely a laboratory designation that does not clearly define the product in the claimed method since different laboratories may use the same laboratory designation to define completely distinct antibody.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamamoto *et al* (Endocrinology 138(1): 383-388; PTO 892).

Yamamoto *et al* teach a method of increasing low vasopressin level in a patient such as rat by administering to said patient at least one substance such as PTHrP(1-34) fragment (See Fig 1, in particular). The reference PTHrP inherently competes and thereby inhibiting the binding of the full length PTHrP to a receptor such as PTHrP receptor and PTH receptor and thereby increasing the vasopressin level (See page 387, column 2, third paragraph, in particular). The reference further teaches a method of maintaining vasopressin level by administering to said patient a substance such as a competitive antagonist to PTHrP such as PTHrP(7-34) (See Fig 2, page 387, column 2, last paragraph, in particular). The reference further teaches that arginine-vasopressin (AVP) has anti-diuretic and pressor activity and is produced from hypothalamic magnocellular neurons in the suproptic nucleic (SON) and paraventricular nuclei of the brain (See page 383, column 2, second paragraph, in particular). Yamamoto et al further teach that centrally administered (icv) causes the secretion of AVP from the thalamus and the plasma AVP levels is similar to the levels observed after the restriction of water and food intake or hyperosmolarity induced by ip injection of hyperosmotic saline (See page 387, column 2, second paragraph, in particular). Thus, the reference teachings anticipate the claimed invention.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 3-4, and 7-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto *et al* (Endocrinology 138(1): 383-388; PTO 892) in view of Sato *et al* (J Bone Miner Res 8(7): 849-60, 1993; PTO 1449), Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harobr, NY, pages 626-629) and Hotta et al (Endocr J 45(6): 773-8, Dec 1998; PTO 892).

The teachings of Yamamoto *et al* have been discussed supra.

The claimed invention in claim 3 differs from the teachings of the reference only that the method wherein the substance is an anti-PTHrP antibody.

The claimed invention in claim 4 differs from the teachings of the reference only that the method wherein the substance is at least one of a fragment of an anti-PTHrP antibody and a modified form of the fragment.

The claimed invention in claim 7 differs from the teachings of the reference only that the method wherein the substance is a monoclonal anti-PTHrP antibody.

The claimed invention in claim 8 differs from the teachings of the reference only that the method of any one of claims 1 to 4, wherein the low vasopressin level results from cancer.

Sato *et al* teach malignancy associated hypercalcemia is mainly caused by excessive production of parathyroid hormone related protein (PTHrP) by tumor (See abstract, in particular). The symptoms of excess PTHrP include hypercalcemia, cachexia that is associated with polyuria, dehydration and hyperosmolarity due to hypercalcemia, and increasing osteoclastic bone resorption (See 849, in particular). Sato *et al* teach daily SC injection of anti-PTHrP 1-34 monoclonal antibody which inhibiting the binding between PTHrP and its receptor led to a decrease in serum calcium, increase in body weight and survival of nude mice bearing PTHrP producing tumors (See abstract, in particular). Sato et al teach that if a human monoclonal antibody against PTHrP(1-34) could be develop, then passive immunization would be potentially one of the most effective therapies associated with hypercalcemia due to excessive production of PTHrP.

Harlow et al teach a method of producing antibody fragment (See page 626-629, in particular). Harlow *et al* further teach that the problems of using multivalent antibodies on mammalian cells often will lead to capping and internalization of the antigen which can be overcome by using fragments of antibodies (See page 626 in particular).

Hotta et al teach hypercalcemia in euthyroid patient with secondary hypoadranalism and diabetes insipidus due to hypothalamic tumor is associated with decrease in arginine vasopressin

and symptoms caused by a decrease in vasopressin level includes polyuria, severe dehydration, disturbance of thirst sensation caused by the hypothalamic tumor (See abstract, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the substance that inhibits the binding between PTHrP and a receptor as taught by Yamamoto et al for the substance such as the monoclonal antibody that binds to PTHrP(1-34) as taught by Sato et al or PTHrP(1-34) antibody fragment produced by method as taught by Harlow et al for a method of maintaining or increasing low vasopressin level as taught by Yamamoto et al and Sato et al or to treat symptoms associated with increased hypercalcemia and decrease in vasopressin level as taught by Hotta et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Yamamoto et al teach that centrally administered (icv) PTHrP (1-34) causes the secretion of AVP from the thalamus and the plasma AVP levels is similar to the levels observed after the restriction of water and food intake or hyperosmolarity induced by ip injection of hyperosmotic saline (See page 387, column 2, second paragraph, in particular). Sato *et al* teach malignancy associated hypercalcemia is mainly caused by excessive production of parathyroid hormone related protein (PTHrP) by tumor (See abstract, in particular) and monoclonal antibody to PTHrP (1-34) inhibits the binding between PTHrP and its receptor led to a decrease in serum calcium, increase in body weight and survival of nude mice bearing PTHrP producing tumors (See abstract, in particular). Hotta et al teach hypercalcemia in euthyroid patient with secondary hypoadranalism and diabetes insipidus due to hypothalamic tumor is associated with arginine vasopressin and symptoms caused by a decrease in vasopressin level includes polyuria, severe dehydration, disturbance of thirst sensation caused by the hypothalamic tumor (See abstract, in particular). Harlow *et al* further teach that the problems of using multivalent antibodies on mammalian cells often will lead to capping and internalization of the antigen which can be overcome by using fragments of antibodies (See page 626 in particular).

17. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto *et al* (Endocrinology 138(1): 383-388; PTO 892) in view of Sato *et al* (J Bone Miner Res 8(7): 849-60, 1993; PTO 1449), Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harobr, NY, pages 626-629) and Hotta *et al* (Endocr J 45(6): 773-8, Dec 1998; PTO 892) as applied to claims 1, 3-4, and 7-11 and further in view of US Pat No. 6,180,370B (filed June 1995; PTO 892).

The combined teachings of Yamamoto *et al*, Sato *et al*, Harlow *et al* and Hotta *et al* have been discussed supra.

The claimed invention in claim 5 differs from the combined teachings of the references only that the method wherein the substance is a humanized or chimeric antibody.

The '370 patent teaches a method of producing chimeric antibodies (See column 55 lines 25-59; column 59, lines 65, in particular) and humanized antibodies (See column 44 line 33; column 68 lines 8-44, in particular). The '370 patent further teaches that humanized immunoglobulin (antibodies) specifically reactive with strong affinity to a predetermined antigen and remain nonimmunogenic in humans and yet be easily and economically produced in a manner suitable for therapeutic formulation and other uses (See column 2, lines 29-34, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to produce humanized or chimeric antibody as taught by the '370 patent using the monoclonal antibody that binds specifically to PTHrP as taught by Sato et al or Harlow et al for a method of maintaining or increasing low vasopressin level as taught by Yamamoto et al and Sato et al or to treat symptoms associated with increased hypercalcemia and decrease in vasopressin level as taught by Hotta et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with an expectation of success to produce chimeric or humanized antibodies because the '370 patent teaches that the chimeric humanized immunoglobulin (antibodies) specifically reactive with strong affinity to a predetermined antigen and remain nonimmunogenic in humans yet be easily and economically produced in a manner suitable for therapeutic formulation and other uses (See column 2, lines 29-34, in particular). Sato et al teach that if a human monoclonal antibody against PTHrP(1-34) could be develop, then passive immunization would be potentially

one of the most effective therapies associated with hypercalcemia due to excessive production of PTHrP.

18. Claim 6 is free of prior art.

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

21. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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